a serine-phosphorylation defective mutant of $p66^{shc}$ is unable to restore a normal stress response in $p66^{shc}$ targeted cells; v) mice carrying the $p66^{shc}$ targeted mutation have prolonged lifespan.--

**In the claims:**

2. (Amended) A nucleic acid molecule according to claim 1 wherein the serine residue is selected from the group consisting of S17, S19, S20, S26, S28, S36, S38, S40, S41, S54, S60, S66, S80 and S120.

3. (Amended) A nucleic acid molecule according to claim 1 wherein the serine residue is selected from the group consisting of S28, S36 and S54.

4. (Amended) A nucleic acid molecule according to claim 1 wherein the serine residue is S36 and is replaced by alanine ($p66^{shc}$S36A)

5. (Amended) A polypeptide encoded by a nucleic acid molecule according to claim 1.

6. (Amended) A replicable vector comprising nucleic acid according to claim 1 operably linked to control sequences to directs its expression.

14. (Amended) A method according to claim 12 wherein said step of disrupting the $p66^{shc}$ pathway causes a mutant $p66^{shc}$ polypeptide to be expressed such that at least one serine residue present in the wild type $p66^{shc}$ is absent or replaced by a different amino acid residue.

15. (Amended) A method according to claim 14 wherein said

serine residue is S36 and is replaced by alanine.

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17. (Amended) A method according to claim 12 wherein said disruption effects the ability of a serine/threonine kinase, p38 or MAPK to phosphorylate $p66^{shc}$.

22. (Amended) A method for increasing cellular resistance to oxidative stess comprising administration of an effective amount of an agent which disrupts $p66^{shc}$ or a step in the $p66^{shc}$ signalling pathway in a pharmaceutically acceptable carrier .

23. (Amended) A method as claimed in claim 22 wherein said agent is an antisense oligonucleotide capable of specifically hybridising to $p66^{shc}$ nucleic acid.

24. (Amended) A method according to claim 23 wherein said antisense oligonucleotide is RNA

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25.(Amended) A method according to claim 23 wherein the $p66^{shc}$ nucleic acid sequence is shown in Fig. 5.

26. (Amended) A method according to claim 22, wherein said agent is an antibody binding domain capable of specifically binding to a $p66^{shc}$ polypeptide or fragment thereof.

27. (Amended) A method as claimed in claim 22 wherein said agent is administered for the treatment of diseases selected from the group consisting of lung emphysema, myocardial infarction, stroke, premature aging, cell senescence, Parkinson's, Alzheimer, cancers and diabetes.

34. (Amended) A method according to claim 32 wherein said step of determining the amount of a compound of the signalling pathway is an enzyme activity assay.

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